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Rosai-Dorfman disease in a symptomatic elderly man

Gaurav Synghal, MD[a], Risha Bhavan[a], Sharad K. Jain, MD[b], and Umesh D. Oza, MD[a]

[a]Department of Radiology, Baylor University Medical Center, Dallas, Texas; [b]Texas Oncology – Denton, Denton, Texas

ABSTRACT

An 81-year-old man presented with anemia, fatigue, weight loss, and recurrent urinary tract infections and was found to have diffuse large adenopathy and infiltrating renal masses. Surgical excision of a lymph node and histologic evaluation led to the diagnosis of Rosai-Dorfman disease, a rare histioproliferative condition that classically presents with enlarged cervical lymph nodes bilaterally. It also can involve additional nodal chains and/or have extranodal manifestations. The condition can self-resolve or have periods of remission and reactivation.

KEYWORDS Anemia; lymphadenopathy; Rosai-Dorfman

Rosai-Dorfman disease (RDD) is a rare histioproliferative disease with an incidence of 100 cases per year in the United States.[1,2] While RDD is typically seen in younger individuals and is often self-limiting, we present an uncommon case of RDD in a symptomatic man.

CASE REPORT

An 81-year-old man presented to a hematologist with fatigue, a 10-pound weight loss, and laboratory findings suggesting anemia of chronic disease with elevated ferritin, decreased total iron binding capacity, decreased iron, and a low-normal iron percent saturation. The patient had multiple negative stool guaiac tests to rule out underlying colon carcinoma. He was started on iron and B12 supplementation, and a bone marrow biopsy showed a normocellular marrow with trilineage hematopoiesis. At the same time, the patient visited his urologist due to persistent urinary tract infections; computed tomography (CT) showed large retroperitoneal lymphadenopathy and soft tissue density infiltrating the kidneys *(Figure 1a, 1b)*. Additional workup revealed an enlarged 3.8 cm supraclavicular lymph node amenable to surgical excision. Upon histopathologic and immunohistochemical evaluation, the lymph node demonstrated marked sinus histiocytosis with co-expression of S100 and CD68, suggesting RDD. Next-generation sequencing demonstrated no targetable mutations, 5% positive PD-L1 expression, and lack of *PDGFRA* expression. Positron emission tomography (PET)/CT helped evaluate the full extent of the patient's disease burden *(Figure 1c)*. The patient was started on corticosteroids with subsequent symptomatic improvement, stable hemoglobin, and improving adenopathy over the course of 12 months of follow-up.

DISCUSSION

RDD is a rare disease characterized by the overproduction of histiocytes and frequently presents with enlarged cervical lymph nodes. Advanced cases involve additional nodal chains or have extranodal manifestations.[3] Our patient had both nodal involvement and extranodal manifestations of anemia and renal involvement. Multisystemic disease is seen in only 19% of cases, with genitourinary involvement being particularly rare, seen in 4% of cases.[2] The patient's age at diagnosis is also atypical, as RDD is more common in younger people with a mean age at diagnosis of 20.6 years.[1,2] Due to the variety of presentations *(Table 1)*,[2–7] the pathophysiology of RDD is not well understood. Current thoughts include viruses acting as inciting factors to cause reactive histiocytosis, but no causative relationship has been proven.[8]

Suspicion for RDD requires correlation of the patient's symptoms and physical exam findings of cervical adenopathy. Imaging can help lead to a diagnosis or find a site amendable to biopsy. On histology, RDD can show emperipolesis with intact lymphocytes, plasma cells, or erythrocytes inside the cytoplasm of histiocytes. Immunohistochemistry findings of CD68 positivity, S100 positivity, and CD1a negativity are helpful to reach the diagnosis.[9] Once a diagnosis has been established, baseline whole-body imaging and baseline labs (complete blood count with differential, comprehensive metabolic panel, C-reactive

Corresponding author: Gaurav Synghal, MD, Department of Radiology, Baylor University Medical Center, 3500 Gaston Avenue, Dallas, TX 75246 (email: Gaurav.Synghal@BSWHealth.org)

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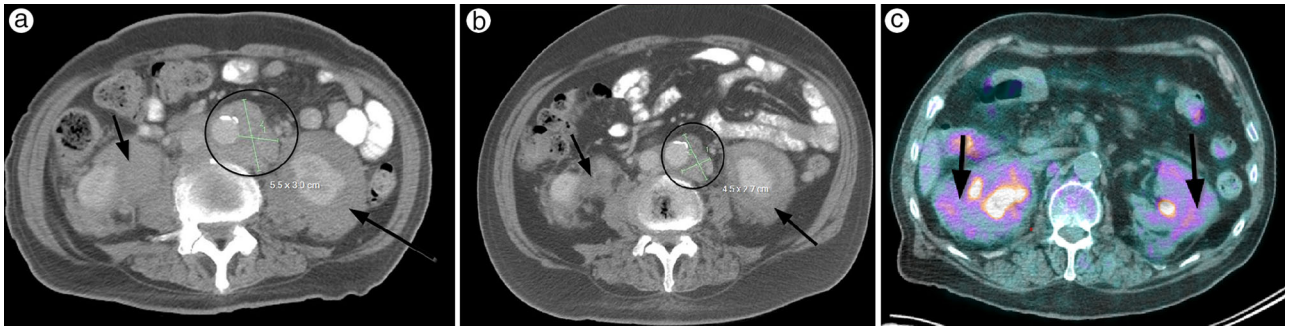

Figure 1. CT of the abdomen and pelvis with intravenous and oral contrast **(a)** prior to treatment and **(b)** following treatment showing decreased size of the paraaortic lymphadenopathy (circle) and perinephric soft tissue rind (arrows). **(c)** PET/CT fusion image. The F-18 FDG accumulation shown in the perinephric soft tissue rind bilaterally is compatible with disease involvement (arrows).

Table 1. Extranodal findings and symptoms of Rosai-Dorfman disease

Organ system	Findings/symptoms
Integumentary	Slow-growing, nonpainful, and nonpruritic discolored nodules, plaques, or papules.[4]
Nervous system	Usually, extra-axial–enhancing dural-based mass, which can result in headaches, seizures, and/or focal weakness.[5]
Cardiovascular	Very rare but can result in a focal cardiac mass, which can present as chest pain.[6]
Pulmonary	Interstitial lung disease or pulmonary nodules, which can result in dyspnea and/or cough.[7]
Genitourinary	Discrete renal lesions or hydronephrosis, which can result in flank pain, hematuria, and/or oliguria.[2,3]
Hematological	Normocytic anemia, leukocytosis, and polyclonal hypergammaglobulinemia, which can result in symptoms such as fatigue and weakness.[2]
Osseous manifestations	Typically, osteolytic intramedullary bone lesions, which result in bone pain.[7]

protein, erythrocyte sedimentation rate, and serologies for HIV and hepatitis) are recommended.[2]

Differential considerations for histiocytic neoplasms include Erdheim-Chester disease, which classically presents with long bone extremity pain, and Langerhans cell histiocytosis, which is more associated with osteolytic bone lesions and upper lobe predominant pulmonary involvement.[10] Unlike RDD, both of these conditions rarely demonstrate adenopathy.[10]

Historically, determining optimal treatment for RDD has been challenging due to the variety of presentations. A consensus recommendation was published in June 2018 to help guide treatment,[2] and new guidelines have been published by the National Comprehensive Cancer Network for histiocytic neoplasms including RDD.[11] Observation is reasonable in most asymptomatic cases, as spontaneous remission has been noted in 20% to 50% of patients.[1,11] Current approaches in symptomatic individuals include corticosteroids, radiotherapy, chemotherapy, and/or immunomodulatory therapy.[1,11] Prognosis tends to be favorable in local disease and more unpredictable in advanced cases with periods of remission and reactivation.[1]

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